UNITED STATES DISTRICT COURT SOUTHERN DISTRICT OF TEXAS HOUSTON DIVISION

STEPHEN McCOLLUM, and SANDRA	§	
McCOLLUM, individually, and STEPHANIE	§	
KINGREY, individually and as independent	§	
administrator of the Estate of LARRY GENE	§	
McCOLLUM,	§	
PLAINTIFFS	§	
	§	
V.	§	CIVIL ACTION NO.
	§	4:14-cv-3253
	§	JURY DEMAND
BRAD LIVINGSTON, JEFF PRINGLE,	§	
RICHARD CLARK, KAREN TATE,	§	
SANDREA SANDERS, ROBERT EASON, the	§	
UNIVERSITY OF TEXAS MEDICAL	§	
BRANCH and the TEXAS DEPARTMENT OF	§	
CRIMINAL JUSTICE.	§	
DEFENDANTS	§	

Plaintiffs' Consolidated Summary Judgment Response Appendix

EXHIBIT 151

Chapter 2

HUMAN ADAPTATION TO HOT ENVIRONMENTS

C. BRUCE WENGER, MD, PhD*

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FACTORS THAT ALTER HEAT TOLERANCE

Heat Acclimatization Physical Fitness, Gender, and Age Drugs and Disease

SUMMARY

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INTRODUCTION

Problems due to heat stress may occur whenever the rate of heat production or heat gain from the environment is sufficiently large in relation to the body's ability to dissipate heat. Thus, sustained high-intensity physical exercise; excessive thermal insulation due to body armor or protective clothing; or thermoregulatory impairment due to fever, drugs, or dehydration may create the conditions for heat-impaired performance or heat illness, even during cool weather.

It is difficult to evaluate the effects of heat stress on the health and performance of troops; thus, the overall impact on military operations is probably much greater than generally appreciated. This is so for several reasons. First, heat illness is probably underreported. Second, in an operational setting, cumulative effects of prolonged heat exposure and combined effects of heat and other stresses are likely to be important, but such effects are difficult and costly to reproduce under controlled experimental conditions. Therefore, they have not been the subject of much experimental study. Third, troops exposed to such conditions may not appreciate the extent to which their abilities and performance are affected.

Most of the earth's hot regions are inhabited, and human physiology permits people to live and work successfully in very hot climates provided they are acclimatized (physiologically adjusted to an environment, in nature) to heat, have access to shade and sufficient supplies of potable water, and can limit their physical activity during the heat of the day. However, military operations in a hot climate must confront problems of heat stress that differ substantially from those ordinarily faced by the local inhabitants. Military operations may involve troops who were not acclimatized to heat before their deployment, and local supplies of fresh water may be insufficient for the requirements of a large military force. Moreover, because of the demands of combat or other mission requirements, troops may have to perform physical exercise during the heat of the day, or at levels that exceed established guidelines for prevention of heat casualties. The accompanying threat to the troops' health and effectiveness may be aggravated by a need to perform such exercise when they are at increased risk of heat illness because they are sleep deprived, or do not have free access to drinking water.

IMPORTANCE OF TISSUE TEMPERATURE

Extreme temperatures injure tissue directly. A protein's biological activity depends on the location of electrical charges in the molecule and on its overall configuration. Many physicochemical processes can alter a protein's configuration and charge distribution, and thus change its activity, without affecting the sequence of amino acids. Such alteration of a protein is called denaturation; and by inactivating a cell's proteins, denaturation injures or kills the cell. High temperature can denature proteins, and a familiar illustration of this effect is the coagulation of the albumin in the white of a cooked egg. If living tissue is heated, injury occurs at temperatures higher than about 45°C, which is also the temperature at which heating the skin causes pain. The degree of injury depends on both temperature and duration of the heating.1

Cold, like heat, can cause direct injury to tissue, although via different mechanisms. As a water-based solution freezes, crystals of pure ice form. Thus all the dissolved substances are left behind in the liquid that has not yet frozen, which becomes more and more concentrated as more ice forms. Freezing damages cells through two mechanisms. First, ice crystals themselves probably disrupt the

cell membranes mechanically. Second, the increase in solute concentration of the cytoplasm as ice forms denatures the proteins by removing their water of hydration, by increasing the ionic strength of the cytoplasm, and by other changes in the physicochemical environment in the cytoplasm.

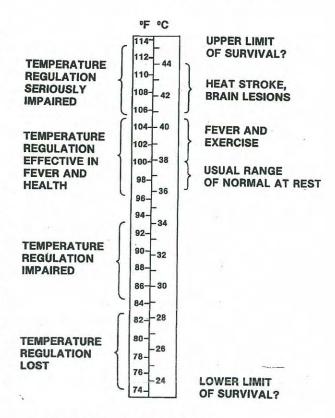
Mammals, including human beings, are homeotherms, or warm-blooded animals, and regulate their internal body temperatures within a narrow band near 37°C (Figure 2-1), despite wide variations in environmental temperature. Tissues and cells can tolerate temperatures from just above freezing to nearly 45°C—a range far wider than the limits within which homeotherms regulate body temperature. What biological advantage do homeotherms gain by maintaining such a stable body temperature?

Temperature is a fundamental physicochemical variable that profoundly affects many biological processes, both through specific effects on such specialized functions as electrical properties and fluidity of cell membranes, and through a general effect on most chemical reaction rates. Most reaction rates vary approximately as an exponential function of temperature within the physiological range, and increasing temperature by 10 Centigrade de-

Human Adaptation to Hot Environments

Fig. 2-1. Ranges of rectal temperature found in healthy persons, patients with fever, and persons with impairment or failure of thermoregulation. Reprinted with permission from Wenger CB. The regulation of body temperature. In: Rhoades RA, Tanner GA. *Medical Physiology*. Boston, Mass: Little, Brown; 1995: 588

grees increases the reaction rate by a factor of 2 to 3. For any reaction, the ratio of the reaction rates at two temperatures 10 Centigrade degrees apart is called the Q_{10} for that reaction, and the effect of temperature on reaction rate is called the Q_{10} effect. The concept of Q_{10} is often generalized to apply to a group of reactions that are thought of as comprising a physiological process because they share a measurable overall effect, such as oxygen consumption. The effect of body temperature on metabolic processes is clinically important in caring for patients with high fevers who are receiving fluid and nutrition intravenously, and an often-used rule states that each Centigrade degree of fever increases a patient's fluid and calorie needs by 13%.²



BODY TEMPERATURES AND HEAT TRANSFER IN THE BODY

The body is divided into a warm internal core and an outer shell (Figure 2-2),3 the temperature of which is strongly influenced by the environment. Although shell temperature is not regulated within narrow limits the way internal body temperature is, thermoregulatory responses do strongly affect the temperature of the shell, and especially its outermost layer, the skin. The shell's thickness depends on the environment and the need to conserve body heat. In a warm environment, the shell may be less than 1 cm thick; but in a subject conserving heat in a cold environment, it may extend several centimeters below the skin. The internal body temperature that is regulated is the temperature of the vital organs inside the head and trunk, which together with a variable amount of other tissue, comprise the warm internal core.

Although heat is produced throughout the body, it is lost only from tissues that are in contact with the environment, mostly skin and respiratory passages. Because heat flows from warmer regions to cooler regions, the greatest heat flows within the body are those from major sites of heat production to the rest of the body, and from core to skin. Within the body, heat is transported by two means: conduction through the tissues; and convection by the

blood, the process by which flowing blood carries heat from warmer tissues to cooler tissues.

Heat flow by conduction is proportional to the thermal conductivity of the tissues, the change of temperature with distance in the direction of heat flow, and the area (perpendicular to the direction of heat flow) through which the heat flows. As Table 2-1 shows, the tissues are rather poor heat conductors

Heat flow by convection depends on the rate of blood flow and the temperature difference between the tissue and the blood supplying the tissue. Because the capillaries have thin walls and, taken together, a large total surface area, the capillary beds are the sites at which heat exchange between tissue and blood is most efficient. Because the shell lies between the core and the environment, all heat leaving the body via the skin must first pass through the shell. Thus the shell insulates the core from the environment. In a cool subject, skin blood flow is low, so that core-to-skin heat transfer is dominated by conduction; the subcutaneous fat layer adds to the insulation value of the shell, because it adds to the thickness of the shell and because fat has a conductivity only about 0.4 times that of dermis or muscle. In a warm subject, on the other hand, the

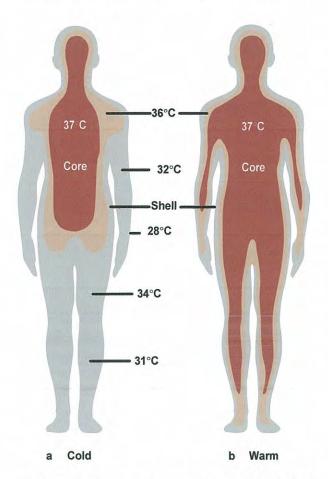


Fig. 2-2. Distribution of temperatures within the body and division of the body into core and shell during exposure to (a) cold and (b) warm environments. The temperatures of the surface and the thickness of the shell depend on the environmental temperature, so that the shell is thicker in the cold and thinner in the heat. Adapted with permission from Elizondo RS. Regulation of body temperature. In: Rhoades RA, Pflanzer RG, eds. Human Physiology. Philadelphia, Pa: Saunders College Publishing; 1989: 823–840.

shell is relatively thin, and thus provides little insulation. Furthermore, a warm subject's skin blood flow is high, so that heat flow from the core to the skin is dominated by convection. In these circumstances the subcutaneous fat layer—which affects conduction but not convection—has little effect on heat flow from core to skin.

Core Temperature

Core temperature varies slightly from one site to another, depending on such local factors as metabolic rate and blood supply and the temperatures of neighboring tissues. However, the notion of a

TABLE 2-1
THERMAL CONDUCTIVITIES AND RATES
OF HEAT FLOW*

	Conductivity	Rate of Heat Flow		
	kcal/(s•m•°C)	kcal/h	Watts	
Copper	0.092	33,120	38,474	
Epidermis	0.00005	18	21	
Dermis	0.00009	32	38	
Fat	0.00004	14	17	
Muscle	0.00011	40	46	
Water	0.00014	51	59	
Oak (across grain)	0.00004	14	17	
Dry air	0.000006	2.2	2.5	
Glass fiber insulation	0.00001	3.6	4.2	

*Through slabs of different materials 1 m² in area and 1 cm thick, with a difference in temperature of one Centigrade degree between the two faces of the slab

Adapted with permission from Wenger CB. The regulation of body temperature. In: Rhoades RA, Tanner GA, eds. *Medical Physiology*. Boston, Mass: Little, Brown; 1995: 590.

single uniform core temperature is a useful approximation because temperatures at different places in the core are all similar to the temperature of the central blood, and they tend to change together. Sites where core temperature is measured clinically include the mouth, the tympanic membrane, the rectum, and occasionally, the axilla. No site is ideal in every respect, and each has certain disadvantages and limitations (Exhibits 2-1 and 2-2).

The value of 98.6°F that is often given as the normal level of body temperature may suggest that body temperature is regulated so precisely that it is not allowed to deviate even a few tenths of a degree. In fact, 98.6°F is simply the Fahrenheit equivalent of 37°C; and, as Figure 2-1 indicates, body temperature does vary. The effects of heavy exercise and fever, for example, are quite familiar. In addition, variation among individuals and such factors4 as time of day (Figure 2-3), phase of the menstrual cycle,5,6 and acclimatization to heat can cause differences of up to about one Centigrade degree in core temperature in healthy subjects at rest. The thermoregulatory system receives information about the level of core temperature provided by temperature-sensitive neurons and nerve endings in the abdominal viscera, great veins, spinal cord, and especially the brain. 7,8 Later in the chapter we

Human Adaptation to Hot Environments

EXHIBIT 2-1

MEASURING BODY CORE TEMPERATURE

Any measurement that is used as an index of core temperature should not be biased by environmental temperature. Because the tongue is richly supplied with blood, oral temperature under the tongue is usually similar to blood temperature and is 0.3°C to 0.4°C below rectal temperature¹; but cooling of the face, neck, or mouth can make oral temperature misleadingly low.² Oral temperature should not be used to assess a patient with a suspected heat illness because such a patient may hyperventilate, thus cooling the mouth.

In 1959, Benzinger introduced tympanic temperature as an index of internal temperature for research in thermal physiology³ and later also advocated its use as a clinical tool.⁴ As Benzinger demonstrated, tympanic temperature responds more rapidly than rectal temperature to body cooling or heating5; and for this reason it has certain advantages over rectal temperature as a research tool. However, Benzinger did not merely say that tympanic temperature responds more rapidly than rectal temperature; he called it "cranial" temperature^{5,6} and claimed that it represented hypothalamic temperature. He claimed further that the tympanum and hypothalamus share "a common blood supply ... from the internal carotid artery," (7(p139) although, in fact, the blood supply of the tympanum is chiefly through branches of the external carotid artery. It would be easy to conclude that Benzinger believed tympanic temperature to be superior to core temperature measured anywhere outside the head (eg, in the esophagus or the heart or great vessels) as a representative of hypothalamic temperature. However, he evidently never claimed that tympanic temperature is superior in this regard to any temperature other than rectal temperature. Nevertheless, later authors8 have concluded that tympanic temperature does indeed represent hypothalamic temperature better than other internal temperature measurements do-without, however, adducing any intracranial temperature measurements to support their conclusion. (Measurements in a surgical patient, in fact, showed that esophageal temperature followed changes in brain temperature more closely than did tympanic temperature.9) As a research tool in thermal physiology, tympanic temperature is now considerably less widely used than esophageal temperature because tympanic temperature is sensitive to skin temperature of the head and neck,2 and thus may be biased substantially by ambient temperature. Benzinger himself recognized this problem and stressed that in environments cooler than 30°C, the ear should be insulated from the environment—preferably with the palm of the subject's hand.5 However, his recommendation has frequently been ignored. Moreover, since most of the tympanum's blood supply comes through branches of the external carotid artery, thus following a somewhat superficial course, it is not clear how wide an area should be insulated, and there is no general agreement on this point.

Infrared sensing devices for measuring tympanic temperature, which eliminate the need for direct contact with the tympanum, have become available in recent years and have been marketed for clinical use. Tympanic temperature has come to enjoy a fair degree of popularity because these devices give a reading quickly and are easy to use. However, these devices are ordinarily used with no provision for insulating the ear from the ambient air, so tympanic temperature may be seriously biased by ambient temperature and is unsuitable for evaluating a patient suspected of having a heat illness. ¹⁰ (For a more extensive critique of tympanic temperature, see Brengelmann. ¹¹)

The rectum is a few tenths of a Centigrade degree warmer than other core sites. The rectum is well insulated from the environment, so rectal temperature is independent of environmental temperature and is the most reliable clinical index of body temperature.

If a patient holds his or her upper arm firmly against the chest so as to close the axilla, its temperature will gradually approach core temperature. Probably the chief advantage of measuring axillary temperature is that disinfecting the thermometer is less critical than when temperature is measured in the mouth or rectum. However, it may take 30 minutes or more for axillary temperature to come reasonably close to core temperature, so axillary temperature may be misleadingly low if insufficient time is allowed or if the patient does not keep his or her arm firmly against the chest. Axillary temperature has all but fallen into disuse.

(1) Cranston WI, Gerbrandy J, Snell ES. Oral, rectal and oesophageal temperatures and some factors affecting them in man. J Physiol (Lond). 1954;126:347–358. (2) McCaffrey TV, McCook RD, Wurster RD. Effect of head skin temperature on tympanic and oral temperature in man. J Appl Physiol. 1975;39:114–118. (3) Benzinger TH. On physical heat regulation and the sense of temperature in man. Proc Natl Acad Sci U S A. 1959;45:645–659. (4) Benzinger TH. Clinical temperature. New physiological basis. JAMA. 1969;209:1200–1206. (5) Benzinger TH, Taylor GW. Cranial measurements of internal temperature in man. In: Hardy JD, ed. Temperature, Its Measurement and Control in Science and Industry. Vol 3, Part 3, Biology and Medicine. New York, NY: Reinhold; 1963: 111–120. (6) Benzinger TH, Kitzinger C, Pratt AW. The human thermostat. In: Hardy JD, ed. Part 3. Biology and Medicine. In: Herzfeld CM, ed. Temperature: Its Measurement and Control in Science and Industry. Vol 3. New York, NY: Reinhold; 1963: 637–665. (7) Benzinger TH. The human thermostat. Sci Am. 1961;204:134–147. (8) Cabanac M, Caputa M. Open loop increase in trunk temperature produced by face cooling in working humans. J Physiol (Lond). 1979;289:163–174. (9) Shiraki K, Sagawa S, Tajima F, Yokota A, Hashimoto M, Brengelmann GL. Independence of brain and tympanic temperatures in an unanesthetized human. J Appl Physiol. 1988;65:482–486. (10) Roberts WO. Assessing core temperature in collapsed athletes: What's the best method? The Physician and Sportsmedicine. 1994;22(8):49–55. (11) Brengelmann GL. Dilemma of body temperature measurement. In: Shiraki K, Yousef MK, eds. Man in Stressful Environments: Thermal and Work Physiology. Springfield, Ill: Charles C Thomas; 1987: 5–22.

EXHIBIT 2-2

BRAIN TEMPERATURE

A few investigators believe in the existence in humans of a physiological process called "selective brain cooling" that keeps the brain cooler than the trunk core during hyperthermia. ^{1,2} A similar process is known to occur in panting animals that possess carotid retes or other specialized vascular structures that provide for heat exchange between carotid arterial blood on its way to the brain, and cool venous blood returning from the respiratory passages, where evaporative cooling takes place. However, panting is not an important heat-loss mechanism in humans, and humans have no such specialized vascular structures for heat exchange. These investigators therefore propose that selective brain cooling in humans depends on venous blood that has been cooled by evaporation of sweat on the skin of the head, and then drains into the cranium ¹⁻³ to exchange heat at several sites, particularly the cavernous sinus. ^{1,2} The evidence for selective brain cooling in humans is based largely on measurements of tympanic temperature, taken as representing brain temperature. In fact, because fanning to cool the face was found to lower tympanic temperature, fanning the face has been recommended as a way to protect the brains of patients with hyperthermia from thermal injury. ⁴ However, humans have no known heat-exchange mechanism that can cool the brain's blood supply more than a few hundredths of a Centigrade degree. ⁵ Interpretation of tympanic temperature as either core temperature or brain temperature is fraught with problems. Moreover, reports that the difference between esophageal and tympanic temperatures can be eliminated by suitable construction and placement of the tympanic temperature probe ⁶ imply that the notion of significant selective brain cooling in humans rests on a measurement artifact.

(1) Cabanac M. Keeping a cool head. News Physiol Sci. 1986;1:41–44. (2) Cabanac M, Caputa M. Natural selective cooling of the human brain: Evidence of its occurrence and magnitude. J Physiol (Lond). 1979;286:255–264. (3) Cabanac M, Brinnel H. Blood flow in the emissary veins of the human head during hyperthermia. Eur J Appl Physiol. 1985;54:172–176. (4) Cabanac M. Face fanning: A possible way to prevent or cure brain hyperthermia. In: Khogali M, Hales JRS, eds. Heat Stroke and Temperature Regulation. Sydney, Australia: Academic Press; 1983: 213–221. (5) Wenger CB. More comments on "Keeping a cool head." News Physiol Sci. 1987;2:150. (6) Sato KT, Kane NL, Soos G, Gisolfi CV, Kondo N, Sato K. Reexamination of tympanic membrane temperature as a core temperature. J Appl Physiol. 1996;80:1233–1239.

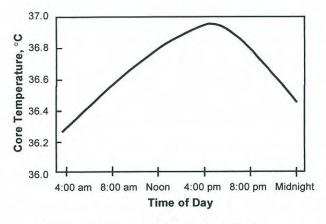


Fig. 2-3. Effect of time of day on internal body temperature of healthy resting subjects. Reprinted with permission from Wenger CB. The regulation of body temperature. In: Rhoades RA, Tanner GA. *Medical Physiology.* Boston, Mass: Little, Brown; 1995: 591. Original data sources: (1) Mackowiak PA, Wasserman SS, Levine MM. A critical appraisal of 98.6°F, the upper limit of normal body temperature, and other legacies of Carl Reinhold August Wunderlich. *JAMA*. 1992;268:1578–1580. (2) Stephenson LA, Wenger CB, O'Donovan BH, Nadel ER. Circadian rhythm in sweating and cutaneous blood flow. *Am J Physiol*. 1984;246:R321–R324.

discuss how the thermoregulatory system processes this information and uses it to maintain core temperature within a narrow range.

Skin Temperature

Skin temperature is important in heat exchange and thermoregulatory control. Most heat is exchanged between the body and the environment at the skin surface. Skin temperature is much more variable than core temperature and is affected by thermoregulatory responses such as skin blood flow and sweat secretion; by the temperatures of underlying tissues; and by environmental factors such as air temperature, air movement, and thermal radiation. Skin temperature, in turn, is one of the major factors determining heat exchange with the environment. For these reasons, skin temperature provides the thermoregulatory system with important information about the need to conserve or lose body heat. Many bare nerve endings just under the skin are very sensitive to temperature. Depending on the relation of discharge rate to temperature, these nerve endings are classified as either warm or cold receptors^{7,9} (Figure 2-4). From the relative densities of cold- and warm-sensitive spots in human skin, 10 cold receptors appear to be roughly 10-fold as nu-

Human Adaptation to Hot Environments

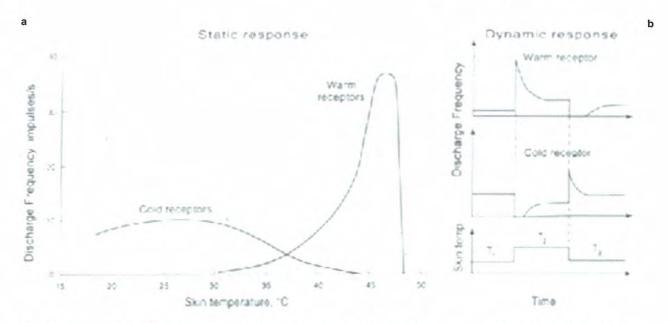


Fig. 2-4. Responses of cold- and warm-sensitive nerve fibers in the skin. Static response (a) is the discharge frequency when skin temperature is stable. Dynamic response (b) is the discharge frequency following a change in skin temperature. Adapted with permission from Hensel H, Kenshalo DR. Warm receptors in the nasal region of cats. *J Physiol (Lond)*. 1969;204:109.

merous as warm receptors because, as a rule, a single cold or warm fiber innervates a single cold-or warm-sensitive spot. With heating of the skin, warm receptors respond with a transient burst of activity, whereas cold receptors respond with a transient suppression; the reverse happens with cooling. These transient responses at the beginning of heating or cooling give the central integrator almost immediate information about changes in skin temperature, and may explain, for example, the intense, brief sensation of being chilled that occurs during a plunge into cold water.

Skin temperature usually is not uniform over the body surface, so a mean skin temperature $(\overline{\boldsymbol{T}}_{sk})$ is frequently calculated from skin temperatures measured at several selected sites, usually weighting the temperature measured at each site according to the fraction of body surface area that it represents. It would be prohibitively invasive and difficult to measure shell temperature directly. Instead, therefore, skin temperature also is commonly used along with core temperature to calculate a mean body temperature and to estimate changes in the amount of heat stored in the body.

BALANCE BETWEEN HEAT PRODUCTION AND HEAT LOSS

All animals exchange energy with the environment. Some energy is exchanged as mechanical work, but most is exchanged as heat—by conduction, convection, and radiation; and as latent heat through evaporation or (rarely) condensation of water (Figure 2-5). If the sum of energy production and energy gain from the environment does not equal energy loss, the extra heat is "stored" in, or lost from, the body. This is summarized in Equation 1, the heat balance equation:

(1)
$$M = E + R + C + K + W + S$$

where M is metabolic rate; E is rate of heat loss by evaporation; R and C are rates of heat loss by radiation and convection, respectively; K is the rate of heat loss by conduction (only to solid objects in practice, as explained later); W is rate of energy loss as mechanical work; and S is rate of heat storage in the body, which takes the form of changes in tissue temperatures. ^{12,13}

The term *M* is always positive, but the other terms in Equation 1 may be either positive or negative. E, R, C, K, and W are positive if they represent energy losses from the body, and negative if they represent

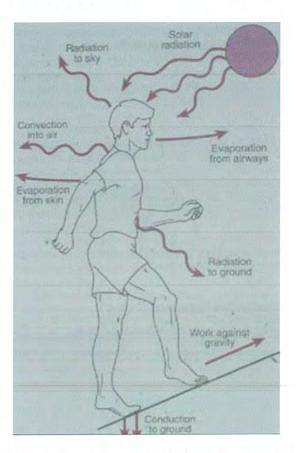


Fig. 2-5. Exchange of energy with the environment. This hiker gains heat from the sun by radiation, and loses heat by conduction to the ground through the soles of his feet, by convection into the air, by radiation to the ground and sky, and by evaporation of water from his skin and respiratory passages. In addition, some of the energy released by his metabolic processes is converted into mechanical work, rather than heat, since he is walking uphill. Reprinted with permission from Wenger CB. The regulation of body temperature. In: Rhoades RA, Tanner GA, eds. *Medical Physiology*. Boston, Mass: Little, Brown; 1995: 592.

energy gains. When S = 0, the body is in heat balance and body temperature neither rises nor falls. When the body is not in heat balance, its mean tissue temperature increases if S is positive, and decreases if S is negative. This commonly occurs on a short-term basis and lasts only until the body responds to changes in its temperature with thermoregulatory responses sufficient to restore balance; but if the thermal stress is too great for the thermoregulatory system to restore balance, the body will continue to gain or lose heat, until either the stress diminishes so that the thermoregulatory system can again restore the balance, or death occurs (Exhibit 2-3).

EXHIBIT 2-3 UNITS FOR MEASURING QUANTITY OF HEAT

The International Union of Physiological Sciences endorses the International System of Units (Système Internationale, SI) for expressing physiological quantities. In this system, quantity of heat is expressed in joules, the unit of work, and rate of heat production or heat flow is expressed in watts, the unit of power (1 W = 1 J/s). In traditional physiological usage, however, heat is expressed in kilocalories (kcal), which are still used widely enough that it is useful to be familiar with them. A kilocalorie (1 kcal = 4186 J) is the quantity of heat that will raise the temperature of 1 kg of pure water by one Centigrade degree, and is identical to the calorie (often spelled with a capital C) used to express the energy value of foods. The word "calorie," however, is a potential source of confusion because the same word was used in chemistry and physics to refer to a unit only 0.001 as large (sometimes called a small calorie), which is the quantity of heat that will raise the temperature of 1 g of pure water by one Centigrade degree.

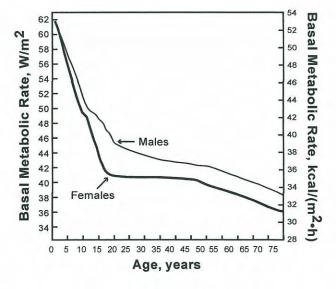


Fig. 2-6. Effects of age and gender on basal metabolic rate of normal subjects, expressed as the ratio of energy consumption to body surface area. Original data source: Fleish PA. La métabolisme basal standard et sa détermination au moyen du "metabocalculator." *Helv Med Acta.* 1951; 18:23–44.